# DERIVATIVES OF PIPERAZINE. XVI.
# THE ADDITION OF 1-ARYLPIPERAZINES TO 1,2-EPOXY-3-ARYLOXYPROPANES

By

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# PREFACE

The subject matter of this dissertation is presented in two sections. In the first section the synthesis of the intermediate 1-arylpiperazines and 1,2-epoxy-3-aryloxypropanes are presented. The second section consists of a general discussion of the addition of amines to 1,2-epoxides followed by the preparation procedure and properties of the 1-aryl-4-(2-hydroxy-3-aryloxypropyl) piperazines prepared.

The manner of listing technical works is the customary one used by the journals of the American Chemical Society. The abbreviations of journals are those adopted by Chemical Abstracts.

All temperatures are reported in degrees Centigrade, and the Centigrade symbol is omitted. Melting points are corrected and were determined with a thermometer calibrated against a Bureau of Standards corrected thermometer.

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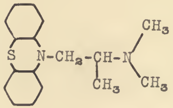
# CHAPTER I

# INTRODUCTION

The importance of therapeutically active synthetic chemical compounds to the well being of man is incalculable. The range of application of these materials appears to have no limit, for there is virtually no phase of medicine in which the synthetics have not been utilized with some degree of success.

The purpose of this work was to produce compounds which might exhibit some type of desirable physiological action. Examination of a large number of currently used pharmaceuticals shows that their structures frequently contain diamine, amino ether, or amino alcohol groups. A few examples illustrating the wide physiological spectrum of drugs containing these groups are:

(a) Phenergan Base,*

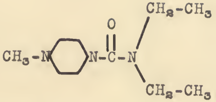


a diamine prepared by Charpentier[1,2] and Huttrer,[3] is used for symptomatic relief of allergic disorders.

---

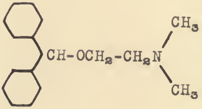
*Registered Trademark

(b) Hetrazan,*



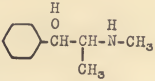
a piperazine derivative prepared by Kushner, et. al.,[4] is effective against filariasis, loaiasis, and onchocerciasis.

(c) Benadryl,*



an amino ether prepared by Rieveschl,[5,6] is considered a standard in the field of antihistaminics.

(d) -Ephedrine,



is a naturally occurring amino alcohol, now usually prepared by the synthesis of Neubert, et. al.[7,8] It is used for asthma, allergic disorders, shrinking the mucosa of the nose, and dilation of the pupils.

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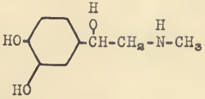
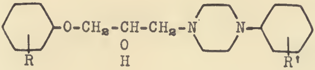
*Registered Trademark

(e) Adrenaline,



is an amino alcohol isolated from animal adrenal glands by Takamine,[9,10] Aldrich,[11] von Furth,[12] and Abel.[13] Its structure was shown by Pauly;[14,15] it was synthesized by Stolz;[16] its optical isomers were resolved by Flacher.[17,18] Adrenaline is used for asthma, acute allergic states, shock, and for localizing the action of anesthetics.

Consideration of these and other similar pharmaceuticals led to the preparation of a series of 1-aryl-4-(2-hydroxy-3-aryloxypropyl) piperazines whose structures



R = (H, Cl, $CH_3$, $CH_3O$)

R' = (H, Cl, $CH_3$)

contain the diamine, amino ether, and amino alcohol groups discussed previously.

This dissertation describes the preparation and physical properties of these compounds.

All of the new compounds prepared during this research project will be submitted to Parke-Davis and Company for physiological testing. Reports of these testing programs will be utilized in further synthetic studies.

# CHAPTER II

# PREPARATION OF INTERMEDIATES

## A. 1-Arylpiperazines

### 1. General Discussion

The synthesis of 1-arylpiperazines has been carried out by numerous methods. The two most practical methods for the laboratory preparation of these compounds in sizable quantities are those of Pollard, et. al.,[19,20] and Prelog, et. al.[21,22]

The method of Pollard, et. al.[19,20] consists of heating an aryl amine hydrochloride with diethanolamine hydrochloride for a period of six to eight hours at 220-240° to yield the dihydrochloride of the 1-arylpiperazine. This dihydrochloride is then neutralized to produce the free amine.

In the method of Prelog, et. al.,[21,22] the free aryl amine together with a bis-$\beta$-haloethylamine hydrohalide are refluxed with methanol or butanol for twelve to sixteen hours to give the hydrohalide salt of the 1-arylpiperazine from which the free base is released by neutralization.

The procedure of Pollard, et. al.[19,20] was chosen for the preparation of the 1-arylpiperazines because the starting materials required were commercially available and the reaction time is much shorter than that of Prelog, et. al.[21,22]

### 2. Experimental

The following 1-arylpiperazines were prepared:

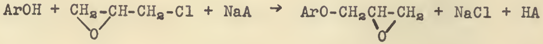
1-Phenylpiperazine
1-(2-Chlorophenyl) piperazine
1-(3-Chlorophenyl) piperazine
1-(4-Chlorophenyl) piperazine
1-(2-Methylphenyl) piperazine
1-(3-Methylphenyl) piperazine
1-(4-Methylphenyl) piperazine

## B. 1,2-Epoxy-3-aryloxypropanes

### 1. General Discussion

All of the widely used methods for the preparation of 1,2-epoxy-3-aryloxypropanes involve the reaction of a phenol with epichlorohydrin or glycerol dichlorohydrin.

In 1891, Lindeman[23] showed that the reaction of epichlorohydrin with a sodium phenate yielded 1,2-epoxy-3-aryloxypropane. Other investigators who used epichlorohydrin and a phenol were Boyd and Marle[24] in 1908, Marle[25] in 1912, Forneau, et. al.,[26] in 1928, Fairbourne, et. al.,[27] in 1932, Slagh and Alquist[28,29] in 1939, Newman, et. al.,[30] in 1947, Geigy[31] in 1947, and Shell Development Company[32] in 1949. In all of these cases the reaction occurs according to the following equation:

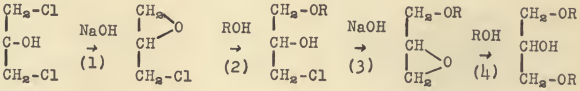


$$ArOH + \underbrace{CH_2-CH}_{O}-CH_2-Cl + NaA \rightarrow ArO-CH_2\underbrace{CH-CH_2}_{O} + NaCl + HA$$

(Ar = Aryl)

(A = $OH^-$ or other $H^+$ acceptor)

Fairbourne, et. al.,[27,33] found that the reaction of glycerol dichlorohydrin, sodium hydroxide, and an alcohol or phenol takes place in the following four steps:



(R = $CH_3$-, $C_2H_5$-, or $C_6H_6$-)

They have shown that the reaction of equimolar quantities of sodium hydroxide and glycerol dichlorohydrin in the presence of the alcohol gives about ninety percent conversion to epichlorohydrin (1). Steps (2) and (3) did not occur to any extent until another equivalent quantity of sodium hydroxide was added. The progress of step (4) could be kept to a minimum by limiting the amount of alcohol. These results indicated that there should be little difference in the yield of epoxides in reactions using either epichlorohydrin or glycerol dichlorohydrin. This conclusion is substantiated by comparison of the results reported on the two methods.

## 2. Experimental

The method employed for the preparation of the 1,2 epoxy-3-aryloxypropanes was essentially that suggested by the Shell Development Company.[32] The following epoxides were prepared:

1,2 Epoxy-3-phenoxypropane
1,2 Epoxy-3-(2-chlorophenoxy) propane
1,2 Epoxy-3-(4-chlorophenoxy) propane
1,2 Epoxy-3-(2-methylphenoxy) propane
1,2 Epoxy-3-(3-methylphenoxy) propane
1,2 Epoxy-3-(4-methylphenoxy) propane
1,2 Epoxy-3-(1-naphthoxy) propane
1,2 Epoxy-3-(4-methoxyphenoxy) propane

All of these with the exception of 1,2-epoxy-3-(4-methoxyphenoxy) propane have been prepared by previous investigators.

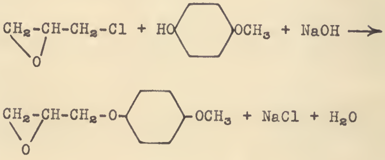
The preparation and physical properties of 1,2-epoxy-3-(4-methoxyphenoxy) propane are subsequently described since no reference to this compound was found in the literature.

## C. 1,2-Epoxy-3-(4-methoxyphenoxy) propane

In a five-liter three-necked flask equipped with mechanical stirrer, addition funnel, and thermometer, were placed 4-methoxyphenol (1000 g., 8.05 mols.) and epichlorohydrin (925 g., 10 mols.). Sodium hydroxide (322 g., 8.05 mols.) in 500 g. of water was then added to the stirred mixture at such a rate that the reaction temperature was kept between 70 and 80°. The addition required about ninety minutes. After the addition was complete, the reaction mixture was heated to 100° for one hour, cooled to room temperature, and extracted with benzene. The benzene extract was dried over anhydrous sodium sulfate overnight. Removal of the low-boiling materials was then carried out at water pump vacuum. Distillation of the residue gave 1,2-epoxy-3-(4-methoxyphenoxy) propane (893 g., 51%) boiling at 135-7° at 2.5 mm.

## 1,2-Epoxy-3(4 methoxyphenoxy)propane

Equation for Synthesis:



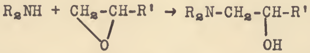
| | |
|---|---|
| Molecular Formula | $C_{10}H_{12}O_3$ |
| Molecular Weight | 180.20 |
| Boiling Point | 135-7/2.5 mm. |
| Melting Point | 47-48 |
| Yield of Product | 51% |

# CHAPTER III

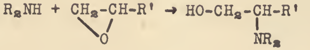
## REACTION OF 1-ARYLPIPERAZINES WITH 1,2-EPOXY-3-ARYLOXYPROPANES

### A. General Discussion

The reaction of ammonia or amines with 1,2-epoxides has been widely investigated. This condensation was described as early as 1860 by Würtz[34] who investigated the reaction of ammonia with ethylene oxide. Monosubstituted ethylene oxides would be expected to react with ammonia or amines according to either or both of the following equations:

(1) 

$$R_2NH + \underset{\diagdown\,O\,\diagup}{CH_2\text{-}CH}\text{-}R' \rightarrow R_2N\text{-}CH_2\text{-}\underset{OH}{\underset{|}{CH}}\text{-}R'$$

(2) 

$$R_2NH + \underset{\diagdown\,O\,\diagup}{CH_2\text{-}CH}\text{-}R' \rightarrow HO\text{-}CH_2\text{-}\underset{NR_2}{\underset{|}{CH}}\text{-}R'$$

Krassousky[35] studied these reactions extensively and found that they proceeded according to equation (1) to produce the secondary amino alcohol. Castro and Noller[36] have shown that the product of the reaction of benzylethylene oxide and ammonia is identical with that formed by the reduction of the condensate of nitromethane and phenylacetaldehyde and is, therefore, 1-phenyl-3-amino-2-propanol.

Boyd and Knowlton,[37] Boyd,[38] and Stephens[39] have also shown that this reaction yields the secondary amino alcohol.

Catalytic amounts of water have been found necessary for the reaction in some cases.[35,40,41] Bradley and Stephenson,[42] however, prepared numerous derivatives from 1,2-epoxy-3-aryloxypropanes and aliphatic amines in the absence of water.

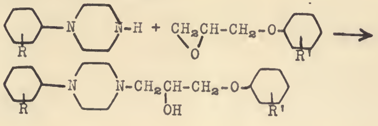
The many variations in procedure reported for the addition of amines to epoxides make it apparent that the rate of reaction is highly dependent upon the nature of the substitution of the amine as well as that of the epoxide.

## B. Experimental

The general procedures employed for the synthesis of the 1-aryl-4-(2-hydroxy-3-aryloxypropyl) piperazines are subsequently described. These procedures are followed by individual data sheets which tabulate the preparation procedure, recrystallizing solvent, yield, and certain physical properties of each piperazine prepared.

1-Aryl-4-(2-hydroxy-3-aryloxypropyl) piperazine

Equation for Synthesis:



Procedure I

1-Arylpiperazine (0.10 mol.) and 1,2-epoxy-3-aryloxypropane (0.10 mol.) were mixed thoroughly in a 125-ml. Erlenmeyer flask. After standing 24 hours, the reaction was essentially complete. The product at this point was either crystalline or of the consistency of barely molten glass. When crystallization did not occur spontaneously, it was induced either by scratching the container with a glass rod or by seeding.[a] The impure crystalline product was then purified by repeated crystallization from an appropriate solvent until the mother liquor obtained was colorless and the melting point range of the product was 1° or less.

Procedure II

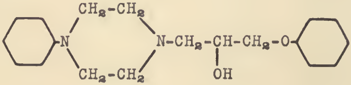
1-Arylpiperazine (0.10 mol.) was completely dissolved in 50 ml. of 95% ethanol in a 250 ml. Erlenmeyer flask. 1,2-Epoxy-3-aryloxypropane (0.10 mol.) was then added and the mixture shaken until it was homogeneous. After standing 12 hours the reaction was essentially complete. When crystallization of the product had not occurred at this point, it was induced either by scratching the container with a glass rod or by seeding.[a] The impure crystalline product was purified by repeated crystallization from an appropriate solvent until the mother liquor obtained was colorless and the melting point range of the product was 1° or less.

---

[a] Seed was obtained by treating small portions of a concentrated ethanolic solution of the non-crystalline product with crystals of different homologs until one was found which induced crystallization.

## 1-Phenyl-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . . . . . . . . .I, page 13

Recrystallizing Solvent . . . . . . . . . . . . .Ethanol

Yield, %. . . . . . . . . . . . . . . . . . . . . . . . . 79

Molecular Formula . . . . . . . . . . . . . . . . . .$C_{19}H_{24}N_2O_2$

Molecular Weight. . . . . . . . . . . . . . . . . . . 276.37

Melting Point . . . . . . . . . . . . . . . . . . . . . 124.5-125

Analytical Data:

Carbon, %:

Calculated: 73.04

Found: 73.30

Hydrogen, %:

Calculated: 7.74

Found: 7.65

Solubilities:

Ethanol . . . . . . . . .Slightly soluble

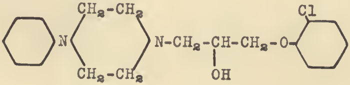
Chloroform. . . . . . . .Soluble

Benzene . . . . . . . . .Moderately soluble

Water . . . . . . . . . .Insoluble

## 1-Phenyl-4-[2-hydroxy-3-(2-chlorophenoxy)propyl] piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . . . . .I, page 13

Recrystallizing Solvent . . . . . . . . . . . . .Ethanol

Yield, %. . . . . . . . . . . . . . . . . . . . . . 75

Molecular Formula . . . . . . . . . . . . . . . . .$C_{19}H_{23}N_2O_2Cl$

Molecular Weight. . . . . . . . . . . . . . . . . .346.85

Melting Point . . . . . . . . . . . . . . . . . . . 89-90

Analytical Data:

Carbon, %:

Calculated: 65.79

Found: 65.82

Hydrogen, %

Calculated: 6.68

Found: 6.99

Solubilities:

Ethanol . . . . . . . .Moderately soluble

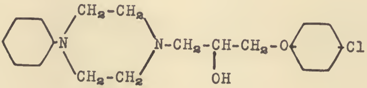
Chloroform. . . . . . .Soluble

Benzene . . . . . . . .Soluble

Water . . . . . . . . .Insoluble

## 1-Phenyl-4-[2-hydroxy-3-(4-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 71 |
| Molecular Formula. | $C_{19}H_{23}N_2O_2Cl$ |
| Molecular Weight. | 346.85 |
| Melting Point | 142-143 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 65.79 |
| Found: | 65.58 |

Hydrogen, %:

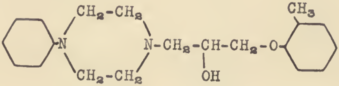
| | |
|---|---|
| Calculated: | 6.68 |
| Found: | 6.85 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-Phenyl-4-[2-hydroxy-3-(2-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 91 |
| Molecular Formula | $C_{20}H_{26}N_2O_2$ |
| Molecular Weight. | 326.43 |
| Melting Point | 104-105 |

Analytical Data:

Carbon, %:

Calculated: 73.58

Found: 73.84

Hydrogen, %:

Calculated: 8.03

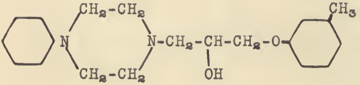
Found: 7.97

Solubilities:

| | |
|---|---|
| Ethanol. | Moderately soluble |
| Chloroform | Soluble |
| Benzene. | Soluble |
| Water. | Insoluble |

## 1-Phenyl-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 74 |
| Molecular Formula | $C_{20}H_{26}N_2O_2$ |
| Molecular Weight. | 326.43 |
| Melting Point | 89.5-90.2 |

Analytical Data:

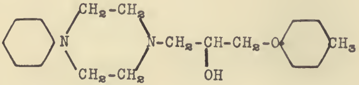
| | | |
|---|---|---|
| Carbon, %: | | |
| | Calculated: | 73.58 |
| | Found: | 73.57 |
| Hydrogen, %: | | |
| | Calculated: | 8.03 |
| | Found: | 7.99 |

Solubilities:

| | |
|---|---|
| Ethanol. | Moderately soluble |
| Chloroform | Soluble |
| Benzene. | Soluble |
| Water. | Insoluble |

## 1-Phenyl-4-[2-hydroxy-3-(4-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Benzene |
| Yield, % | 76 |
| Molecular Formula | $C_{20}H_{26}N_2O_2$ |
| Molecular Weight | 326.43 |
| Melting Point | 130.2-130.9 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 73.58 |
| Found: | 73.70 |

Hydrogen, %:

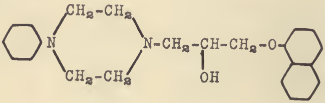
| | |
|---|---|
| Calculated: | 8.03 |
| Found: | 8.12 |

Solubilities:

| | |
|---|---|
| Ethanol | Insoluble |
| Chloroform | Moderately soluble |
| Benzene | Slightly soluble |
| Water | Insoluble |

## 1-Phenyl-4-[2-hydroxy-3-(1-naphthoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Benzene |
| Yield, % | 80 |
| Molecular Formula | $C_{23}H_{26}N_2O_2$ |
| Molecular Weight | 362.46 |
| Melting Point | 105.8-106.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 76.21 |
| Found: | 76.00 |

Hydrogen, %:

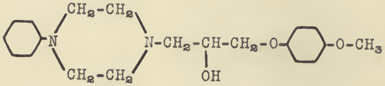
| | |
|---|---|
| Calculated: | 7.23 |
| Found: | 7.19 |

Solubilities:

| | |
|---|---|
| Ethanol | Insoluble |
| Chloroform | Moderately soluble |
| Benzene | Slightly soluble |
| Water | Insoluble |

## 1-Phenyl-4-[2-hydroxy-3-(4-methoxyphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 59 |
| Molecular Formula | $C_{20}H_{26}N_2O_3$ |
| Molecular Weight. | 342.43 |
| Melting Point | 137-138 |

Analytical Data:

Carbon, %:

Calculated: 70.14

Found: 69.88

Hydrogen, %:

Calculated: 7.65

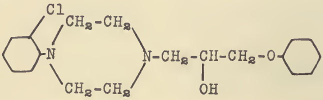
Found: 7.45

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 51 |
| Molecular Formula | $C_{19}H_{23}N_2O_2Cl$ |
| Molecular Weight. | 346.85 |
| Melting Point | 64-65 |

Analytical Data:

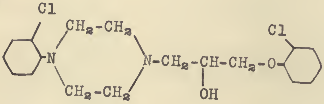
| | | |
|---|---|---|
| Carbon, %: | | |
| | Calculated: | 65.79 |
| | Found: | 65.75 |
| Hydrogen, %: | | |
| | Calculated: | 6.68 |
| | Found: | 7.12 |

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(2-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Cyclohexane |
| Yield, %. | 35 |
| Molecular Formula | $C_{19}H_{22}N_2O_2Cl_2$ |
| Molecular Weight. | 381.30 |
| Melting Point | 99-100.5 |

Analytical Data:

Nitrogen, %:

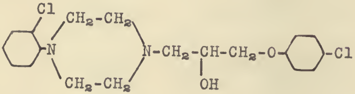
| | |
|---|---|
| Calculated: | 7.35 |
| Found: | 7.53 |

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(4-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 68 |
| Molecular Formula | $C_{19}H_{22}N_2O_2Cl_2$ |
| Molecular Weight | 381.30 |
| Melting Point | 91.8-92.2 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 59.85 |
| Found: | 60.06 |

Hydrogen, %:

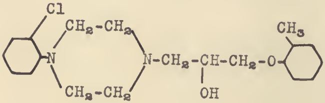
| | |
|---|---|
| Calculated: | 5.82 |
| Found: | 5.75 |

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(2-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Cyclohexane |
| Yield, %. | 41 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 360.88 |
| Melting Point | 76.7-77.7 |

Analytical Data:

Nitrogen, %:

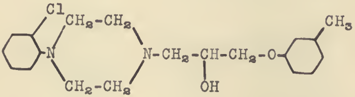
| | |
|---|---|
| Calculated: | 7.59 |
| Found: | 7.41 |

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 57 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight | 360.88 |
| Melting Point | 64-65 |

Analytical Data:

Carbon, %:

Calculated: 66.56

Found: 66.71

Hydrogen, %:

Calculated: 6.98

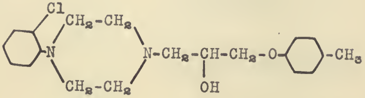
Found: 7.04

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(4-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Cyclohexane |
| Yield, %. | 42 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 360.88 |
| Melting Point | 85.9-86.9 |

Analytical Data:

Nitrogen, %:

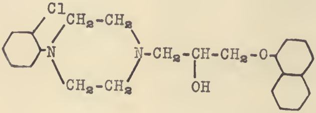
| | |
|---|---|
| Calculated: | 7.60 |
| Found: | 7.32 |

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform. | Soluble |
| Benzene. | Soluble |
| Water | Insoluble |

# 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(1-naphthoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol-Benzene |
| Yield, %. | 75 |
| Molecular Formula | $C_{23}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 396.91 |
| Melting Point | 124-124.6 |

Analytical Data:

Carbon, %:

Calculated: 69.60

Found: 69.69

Hydrogen, %:

Calculated: 6.35

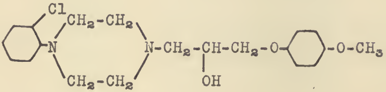
Found: 6.20

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Chlorophenyl)-4-[2-hydroxy-3-(4-methoxyphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 65 |
| Molecular Formula | $C_{20}H_{25}N_2O_3Cl$ |
| Molecular Weight | 376.88 |
| Melting Point | 93-94 |

Analytical Data:

Carbon, %:

Calculated: 63.73

Found: 63.55

Hydrogen, %:

Calculated: 6.69

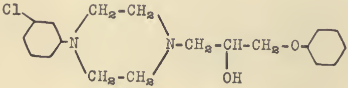
Found: 6.68

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Chlorophenyl)-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 68 |
| Molecular Formula | $C_{19}H_{23}N_2O_2Cl$ |
| Molecular Weight | 346.85 |
| Melting Point | 85-86 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 65.79 |
| Found: | 65.69 |

Hydrogen, %:

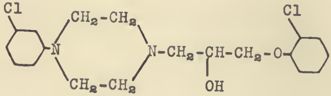
| | |
|---|---|
| Calculated: | 6.68 |
| Found: | 6.51 |

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(2-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 68 |
| Molecular Formula | $C_{19}H_{22}N_2O_2Cl_2$ |
| Molecular Weight | 381.30 |
| Melting Point | 97-98 |

Analytical Data:

Carbon, %:

Calculated: 59.85

Found: 60.01

Hydrogen, %:

Calculated: 5.82

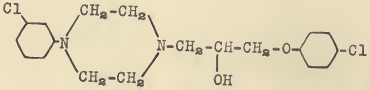
Found: 5.67

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(4-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 72 |
| Molecular Formula | $C_{19}H_{22}N_2O_2Cl_2$ |
| Molecular Weight. | 381.30 |
| Melting Point | 109-109.7 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 59.85 |
| Found: | 59.87 |

Hydrogen, %:

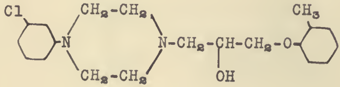
| | |
|---|---|
| Calculated: | 5.82 |
| Found: | 5.74 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

# 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(2-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 71 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight | 360.88 |
| Melting Point | 95-95 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.26 |

Hydrogen, %:

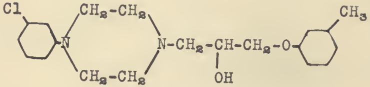
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 6.62 |

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 62 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 360.88 |
| Melting Point | 80.5-81.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.47 |

Hydrogen, %:

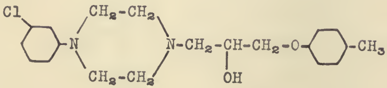
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 7.01 |

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(4-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . . | Ethanol |
| Yield, %. . . . . . . . . . . . . . . . . . . . . . | 61 |
| Molecular Formula . . . . . . . . . . . . . . . | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. . . . . . . . . . . . . . . . | 360.88 |
| Melting Point . . . . . . . . . . . . . . . . . . | 92-93 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.87 |

Hydrogen, %:

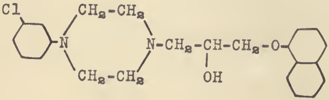
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 7.01 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . . . | Slightly soluble |
| Chloroform. . . . . . . . | Soluble |
| Benzene . . . . . . . . . | Moderately soluble |
| Water . . . . . . . . . . | Insoluble |

## 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(1-naphthoxy) propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol-Benzene |
| Yield, % | 66 |
| Molecular Formula | $C_{23}H_{25}N_2O_2Cl$ |
| Molecular Weight | 396.91 |
| Melting Point | 123-124 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 69.60 |
| Found: | 69.91 |

Hydrogen, %:

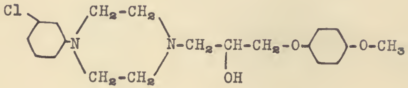
| | |
|---|---|
| Calculated: | 6.35 |
| Found: | 6.38 |

Solubilities:

| | |
|---|---|
| Ethanol | Insoluble |
| Chloroform | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(3-Chlorophenyl)-4-[2-hydroxy-3-(4-methoxyphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 70 |
| Molecular Formula | $C_{20}H_{25}N_2O_3Cl$ |
| Molecular Weight. | 376.88 |
| Melting Point | 106.5-107.5 |

Analytical Data:

Carbon, %:

Calculated: 63.73

Found: 63.57

Hydrogen, %:

Calculated: 6.69

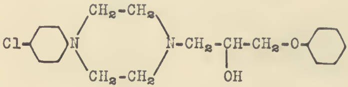
Found: 6.79

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Chlorophenyl)-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . II, page 13

Recrystallizing Solvent . . . . . . . . . . Ethanol-Benzene

Yield, %. . . . . . . . . . . . . . . . . . 69

Molecular Formula . . . . . . . . . . . . . $C_{19}H_{23}N_2O_2Cl$

Molecular Weight. . . . . . . . . . . . . . 346.85

Melting Point . . . . . . . . . . . . . . . 130.8-131.4

Analytical Data:

Carbon, %:

Calculated: 65.79

Found: 65.89

Hydrogen, %:

Calculated: 6.68

Found: 6.68

Solubilities:

Ethanol . . . . . . Slightly soluble

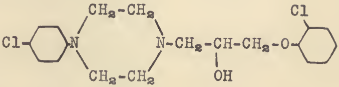
Chloroform. . . . . Soluble

Benzene . . . . . . Moderately soluble

Water . . . . . . . Insoluble

# 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(2-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol-Benzene |
| Yield, % | 79 |
| Molecular Formula | $C_{19}H_{22}N_2O_2Cl_2$ |
| Molecular Weight | 381.30 |
| Melting Point | 111.5-112.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 59.85 |
| Found: | 60.17 |

Hydrogen, %:

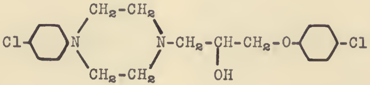
| | |
|---|---|
| Calculated: | 5.82 |
| Found: | 6.05 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(4-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . | II, page 13 |
| Recrystallizing Solvent . . . . . . . . . | Dioxane, Ethanol |
| Yield, %. . . . . . . . . . . . . . . . . . | 53 |
| Molecular Formula . . . . . . . . . . . . . | $C_{19}H_{22}N_2O_2Cl_2$ |
| Molecular Weight. . . . . . . . . . . . . . | 381.30 |
| Melting Point . . . . . . . . . . . . . . . | 154-155 |

Analytical Data:

Carbon, %:

Calculated: 59.85

Found: 59.88

Hydrogen, %:

Calculated: 5.82

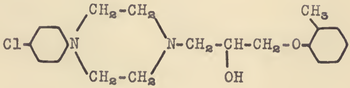
Found: 5.98

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . | Slightly soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . | Slightly soluble |
| Water . . . . . . . . | Insoluble |

## 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(2-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 48 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight | 360.88 |
| Melting Point | 93-94 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 67.02 |

Hydrogen, %:

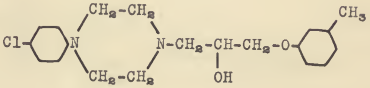
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 6.98 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 67 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 360.88 |
| Melting Point | 106.3-106.6 |

Analytical Data:

Carbon, %:

Calculated: 66.56

Found: 66.67

Hydrogen, %:

Calculated: 6.98

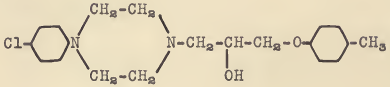
Found: 7.22

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(4-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Benzene |
| Yield, % | 50 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight | 360.88 |
| Melting Point | 144-145 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.75 |

Hydrogen, %:

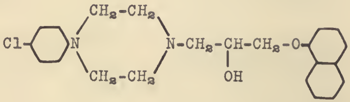
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 7.23 |

Solubilities:

| | |
|---|---|
| Ethanol | Insoluble |
| Chloroform | Soluble |
| Benzene | Slightly soluble |
| Water | Insoluble |

# 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(1-naphthoxy)-propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol-Benzene |
| Yield, % | 53 |
| Molecular Formula | $C_{23}H_{25}N_2O_2Cl$ |
| Molecular Weight | 396.91 |
| Melting Point | 125.3-126 |

Analytical Data:

Carbon, %:

Calculated: 69.60

Found: 69.70

Hydrogen, %:

Calculated: 6.35

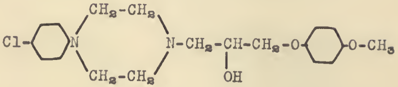
Found: 6.40

Solubilities:

| | |
|---|---|
| Ethanol | Insoluble |
| Chloroform | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Chlorophenyl)-4-[2-hydroxy-3-(4-methoxyphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol-Benzene |
| Yield, %. | 68 |
| Molecular Formula | $C_{20}H_{25}N_2O_3Cl$ |
| Molecular Weight. | 376.88 |
| Melting Point | 143.5-144.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 63.73 |
| Found: | 63.90 |

Hydrogen, %:

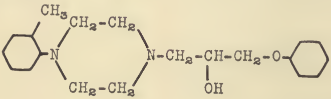
| | |
|---|---|
| Calculated: | 6.69 |
| Found: | 6.50 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(2-Methylphenyl)-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . | Cyclohexane |
| Yield, %. . . . . . . . . . . . . . . . . . . | 48 |
| Molecular Formula . . . . . . . . . . . . . . | $C_{20}H_{26}N_2O_2$ |
| Molecular Weight. . . . . . . . . . . . . . . | 326.42 |
| Melting Point . . . . . . . . . . . . . . . . | 83.6-84.6 |

Analytical Data:

Nitrogen, %:

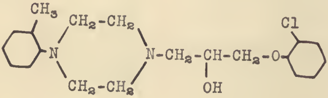
| | |
|---|---|
| Calculated: | 8.58 |
| Found: | 8.68 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . | Soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . | Soluble |
| Water . . . . . . . . | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(2-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Cyclohexane |
| Yield, %. | 42 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 360.88 |
| Melting Point | 83-84 |

Analytical Data:

Nitrogen, %:

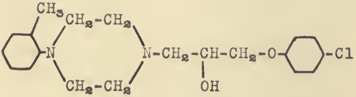
| | |
|---|---|
| Calculated: | 7.60 |
| Found: | 7.65 |

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(4-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 20 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight | 360.88 |
| Melting Point | 94-95 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.72 |

Hydrogen, %

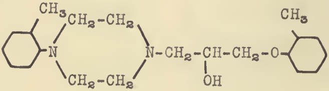
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 7.26 |

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(2-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Cyclohexane |
| Yield, % | 38 |
| Molecular Formula | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight | 340.45 |
| Melting Point | 80.8-82.3 |

Analytical Data:

Nitrogen, %:

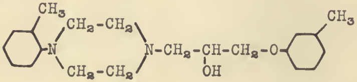
| | |
|---|---|
| Calculated: | 8.23 |
| Found: | 8.29 |

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Cyclohexane |
| Yield, %. | 36 |
| Molecular Formula | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. | 340.45 |
| Melting Point | 57.1-58.6 |

Analytical Data:

Nitrogen, %:

Calculated: 8.23

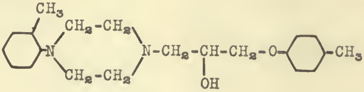
Found: 8.30

Solubilities:

| | |
|---|---|
| Ethanol | Soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(4-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . | Cyclohexane |
| Yield, %. . . . . . . . . . . . . . . . . . . . . | 45 |
| Molecular Formula . . . . . . . . . . . . . . . | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. . . . . . . . . . . . . . . . | 340.45 |
| Melting Point . . . . . . . . . . . . . . . . . . | 75.8-76.3 |

Analytical Data:

Nitrogen, %:

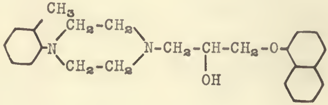
| | |
|---|---|
| Calculated: | 8.23 |
| Found: | 8.19 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . . | Soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . . | Soluble |
| Water . . . . . . . . . | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(1-naphthoxy)-propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . . . . | II, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . . | Ethanol |
| Yield, %. . . . . . . . . . . . . . . . . . . . . . . . | 41 |
| Molecular Formula . . . . . . . . . . . . . . . . | $C_{24}H_{28}N_2O_2$ |
| Molecular Weight. . . . . . . . . . . . . . . . . | 376.48 |
| Melting Point . . . . . . . . . . . . . . . . . . . | 84.8-85.2 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 76.56 |
| Found: | 76.31 |

Hydrogen, %:

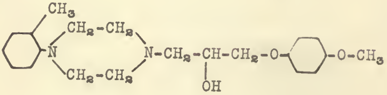
| | |
|---|---|
| Calculated: | 7.50 |
| Found: | 7.63 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . . | Moderately soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . . | Soluble |
| Water . . . . . . . . . | Insoluble |

## 1-(2-Methylphenyl)-4-[2-hydroxy-3-(4-methoxyphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 52 |
| Molecular Formula | $C_{21}H_{28}N_2O_3$ |
| Molecular Weight. | 356.45 |
| Melting Point | 100.0-100.5 |

Analytical Data:

Carbon, %:

Calculated: 70.76

Found: 70.53

Hydrogen, %:

Calculated: 7.92

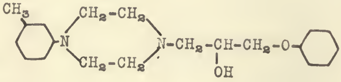
Found: 8.03

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Methylphenyl)-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . . I, page 13

Recrystallizing Solvent . . . . . . . . . . . Ethanol

Yield, %. . . . . . . . . . . . . . . . . . . 55

Molecular Formula . . . . . . . . . . . . . . $C_{20}H_{26}N_2O_2$

Molecular Weight. . . . . . . . . . . . . . . 326.43

Melting Point . . . . . . . . . . . . . . . . 83.5-84.2

Analytical Data:

Carbon, %:

Calculated: 73.58

Found: 73.53

Hydrogen, %:

Calculated: 8.03

Found: 7.91

Solubilities:

Ethanol . . . . . . . Slightly soluble

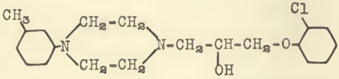
Chloroform. . . . . . Soluble

Benzene . . . . . . . Soluble

Water . . . . . . . . Insoluble

## 1-(3-Methylphenyl)-4-[2-hydroxy-3-(2-chlorophenoxy)propyl] piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 48 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. | 360.88 |
| Melting Point | 79.9-80.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.20 |

Hydrogen, %:

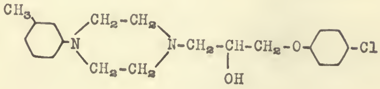
| | |
|---|---|
| Calculated: | 6.98 |
| Found: | 6.77 |

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Methylphenyl)-4-[2-hydroxy-3-(4-chlorophenoxy)propyl]piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . . I, page 13

Recrystallizing Solvent . . . . . . . . . . . Ethanol

Yield, %. . . . . . . . . . . . . . . . . . . . 59

Molecular Formula . . . . . . . . . . . . . . $C_{20}H_{25}N_2O_2Cl$

Molecular Weight. . . . . . . . . . . . . . . 360.88

Melting Point . . . . . . . . . . . . . . . . 113.8-114.1

Analytical Data:

Carbon, %:

Calculated: 66.56

Found: 66.19

Hydrogen, %:

Calculated: 6.98

Found: 7.05

Solubilities:

Ethanol . . . . . . . Slightly soluble

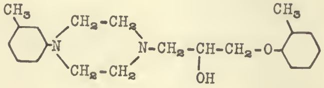
Chloroform. . . . . . Soluble

Benzene . . . . . . . Moderately soluble

Water . . . . . . . . Insoluble

## 1-(3-Methylphenyl)-4-[2-hydroxy-3-(2-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 41 |
| Molecular Formula | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight | 340.45 |
| Melting Point | 81-82 |

Analytical Data:

Carbon, %:

Calculated: 74.08

Found: 73.97

Hydrogen, %:

Calculated: 8.29

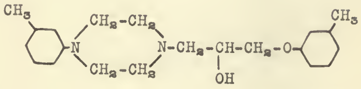
Found: 8.29

Solubilities:

| | |
|---|---|
| Ethanol | Moderately soluble |
| Chloroform | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(3-Methylphenyl)-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . | Ethanol |
| Yield, %. . . . . . . . . . . . . . . . . . . . . . | 58 |
| Molecular Formula . . . . . . . . . . . . . . . | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. . . . . . . . . . . . . . . . | 340.45 |
| Melting Point . . . . . . . . . . . . . . . . . . | 77-77.8 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 74.08 |
| Found: | 73.51 |

Hydrogen, %:

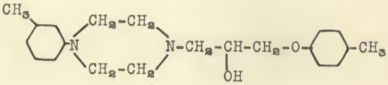
| | |
|---|---|
| Calculated: | 8.29 |
| Found: | 8.26 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . . | Slightly soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . . | Soluble |
| Water . . . . . . . . . | Insoluble |

## 1-(3-Methylphenyl)-4-[2-hydroxy-3-(4-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . . | Ethanol |
| Yield, %. . . . . . . . . . . . . . . . . . . . . | 58 |
| Molecular Formula . . . . . . . . . . . . . . . . | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. . . . . . . . . . . . . . . . . | 340.45 |
| Melting Point . . . . . . . . . . . . . . . . . . | 92.7-93 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 74.08 |
| Found: | 73.75 |

Hydrogen, %:

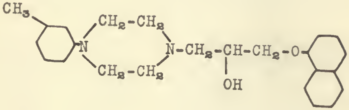
| | |
|---|---|
| Calculated: | 8.29 |
| Found: | 8.26 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . | Slightly soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . | Moderately soluble |
| Water . . . . . . . . | Insoluble |

# 1-(3-Methylphenyl)-4-[2-hydroxy-3-(1-naphthoxy)-propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 70 |
| Molecular Formula | $C_{24}H_{28}N_2O_2$ |
| Molecular Weight. | 376.48 |
| Melting Point | 96.2-96.8 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 76.56 |
| Found: | 76.38 |

Hydrogen, %:

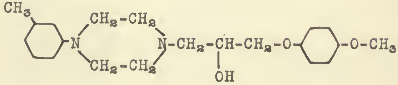
| | |
|---|---|
| Calculated: | 7.50 |
| Found: | 7.74 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(3-Methylphenyl)-4-[2-hydroxy-3-(4-methoxyphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | II, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 62 |
| Molecular Formula | $C_{21}H_{28}N_2O_3$ |
| Molecular Weight. | 356.45 |
| Melting Point | 100-100.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 70.76 |
| Found: | 70.53 |

Hydrogen, %:

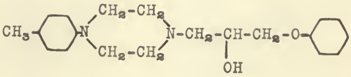
| | |
|---|---|
| Calculated: | 7.92 |
| Found: | 8,03 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Methylphenyl)-4-(2-hydroxy-3-phenoxypropyl)piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . | Ethanol |
| Yield, %. . . . . . . . . . . . . . . . . . . . | 70 |
| Molecular Formula . . . . . . . . . . . . . . | $C_{20}H_{26}N_2O_2$ |
| Molecular Weight. . . . . . . . . . . . . . . | 326.43 |
| Melting Point . . . . . . . . . . . . . . . . | 119-119.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 73.58 |
| Found: | 73.69 |

Hydrogen, %:

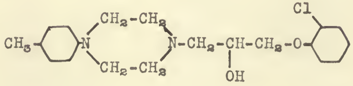
| | |
|---|---|
| Calculated: | 8.03 |
| Found: | 8.14 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . | Slightly soluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . | Moderately soluble |
| Water . . . . . . . . | Insoluble |

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(2-chlorophenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, % | 55 |
| Molecular Formula | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight | 360.88 |
| Melting Point | 87-87.5 |

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 66.56 |
| Found: | 66.36 |

Hydrogen, %:

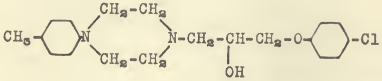
| | |
|---|---|
| Calculated: | 6.98 |
| Found | 7.05 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(4-chlorophenoxy)-propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation . . . . . . . . . . . . . . . . . . | I, page 13 |
| Recrystallizing Solvent . . . . . . . . . . . | Benzene |
| Yield, %. . . . . . . . . . . . . . . . . . . | 55 |
| Molecular Formula . . . . . . . . . . . . . . | $C_{20}H_{25}N_2O_2Cl$ |
| Molecular Weight. . . . . . . . . . . . . . . | 360.88 |
| Melting Point . . . . . . . . . . . . . . . . | 137.8-138.6 |

Analytical Data:

Carbon, %:

Calculated: 66.56

Found: 66.69

Hydrogen, %:

Calculated: 6.98

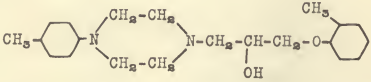
Found: 7.11

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . | Insoluble |
| Chloroform. . . . . . | Soluble |
| Benzene . . . . . . . | Slightly soluble |
| Water . . . . . . . . | Insoluble |

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(2-methylphenoxy)-propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 56 |
| Molecular Formula | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. | 340.45 |
| Melting Point | 97.3-97.8 |

Analytical Data:

Carbon, %:

Calculated: 74.08

Found: 73.76

Hydrogen, %:

Calculated: 8.29

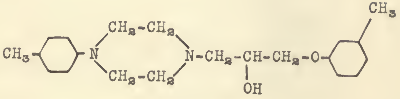
Found: 8.61

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(3-methylphenoxy)propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 57 |
| Molecular Formula | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. | 340.45 |
| Melting Point | 85.6-86.5 |

Analytical Data:

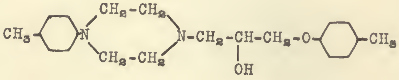
| | | |
|---|---|---|
| Carbon, %: | | |
| | Calculated: | 74.08 |
| | Found: | 74.06 |
| Hydrogen, %: | | |
| | Calculated: | 8.29 |
| | Found: | 8.27 |

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Soluble |
| Water | Insoluble |

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(4-methylphenoxy)-propyl]piperazine

Graphic Formula:



| | |
|---|---|
| Preparation | I, page 13 |
| Recrystallizing Solvent | Ethanol |
| Yield, %. | 56 |
| Molecular Formula | $C_{21}H_{28}N_2O_2$ |
| Molecular Weight. | 340.45 |
| Melting Point | 126-126.7 |

Analytical Data:

Carbon, %:

Calculated: 74.08

Found: 73.93

Hydrogen, %:

Calculated: 8.29

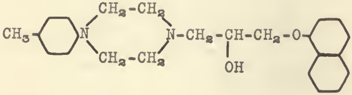
Found: 8.35

Solubilities:

| | |
|---|---|
| Ethanol | Slightly soluble |
| Chloroform. | Soluble |
| Benzene | Moderately soluble |
| Water | Insoluble |

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(1-naphthoxy)-propyl]piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . . II, page 13

Recrystallizing Solvent . . . . . . . . . . . Ethanol

Yield, %. . . . . . . . . . . . . . . . . . . . 57

Molecular Formula . . . . . . . . . . . . . . . $C_{24}H_{28}N_2O_2$

Molecular Weight. . . . . . . . . . . . . . . . 376.48

Melting Point . . . . . . . . . . . . . . . . . 106.8-107.3

Analytical Data:

Carbon, %:

Calculated: 76.56

Found: 76.47

Hydrogen, %:

Calculated: 7.50

Found: 7.56

Solubilities:

Ethanol . . . . . . . Slightly soluble

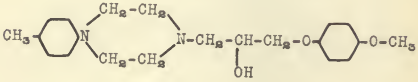
Chloroform. . . . . . Soluble

Benzene . . . . . . . Moderately soluble

Water . . . . . . . . Insoluble

## 1-(4-Methylphenyl)-4-[2-hydroxy-3-(4-methoxyphenoxy)-propyl]piperazine

Graphic Formula:



Preparation . . . . . . . . . . . . . . . . . . II, page 13

Recrystallizing Solvent . . . . . . . . . . . . Ethanol

Yield, %. . . . . . . . . . . . . . . . . . . . 63

Molecular Formula . . . . . . . . . . . . . . $C_{21}H_{28}N_2O_3$

Molecular Weight. . . . . . . . . . . . . . . . 356.45

Melting Point . . . . . . . . . . . . . . . . . 130-131

Analytical Data:

Carbon, %:

| | |
|---|---|
| Calculated: | 70.76 |
| Found: | 70.69 |

Hydrogen, %:

| | |
|---|---|
| Calculated: | 7.92 |
| Found: | 7.97 |

Solubilities:

| | |
|---|---|
| Ethanol . . . . . . . | Slightly soluble |
| Chloroform. . . . . . | Soluble |
| Benzene. . . . . . . | Moderately soluble |
| Water. . . . . . . . . | Insoluble |

## C. Discussion of Experimental Results

The addition of 1-arylpiperazines to 1,2-epoxy-3-aryloxypropanes proceeded spontaneously in contrast to some systems[2,7,8] which required water as a catalyst.

Ortho or meta substitutions on either the phenoxy or phenyl group usually gave products which were lower melting, more soluble, and more difficult to crystallize.

Since the purpose of this research was to produce new compounds for physiological testing, no attempt was made to determine the conditions required for maximum yield. The yields reported in this dissertation are based on the products from which the analytical samples were taken.

# IV. SUMMARY

Fifty-six new 1-aryl-4-(2-hydroxy-3-aryloxypropyl)-piperazines have been prepared by the addition of 1-arylpiperazines to 1,2-epoxy-3-aryloxypropanes. The previously unreported 1,2-epoxy-3-(4-methoxyphenoxy)propane has also been prepared.

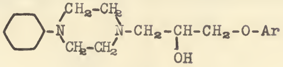
A review of the essential literature has been presented. The general methods by which the compounds were prepared and purified are listed.

An individual sheet, which tabulates significant data, has been included for each compound prepared.

Physical and analytical data for the new compounds are listed in Tables I through VII.

## TABLE I

### DATA ON 1-PHENYL-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES

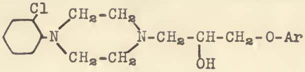


(Ar = Aryl group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | Carbon, % | | Hydrogen, % | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Calcd. | Found | Calcd. | Found |
| Phenyl | $C_{19}H_{24}N_2O_2$ | 276.37 | 124.5-125 | 79 | 73.04 | 73.30 | 7.74 | 7.65 |
| 2-Chlorophenyl | $C_{19}H_{23}N_2O_2Cl$ | 346.85 | 89-90 | 75 | 65.79 | 65.82 | 6.68 | 6.99 |
| 4-Chlorophenyl | $C_{19}H_{23}N_2O_2Cl$ | 346.85 | 142-143 | 71 | 65.79 | 65.58 | 6.68 | 6.85 |
| 2-Methylphenyl | $C_{20}H_{26}N_2O_2$ | 326.43 | 104-105 | 91 | 73.58 | 73.84 | 8.03 | 7.97 |
| 3-Methylphenyl | $C_{20}H_{26}N_2O_2$ | 326.43 | 89.5-90.2 | 74 | 73.58 | 73.57 | 8.03 | 7.99 |
| 4-Methylphenyl | $C_{20}H_{26}N_2O_2$ | 326.43 | 130.2-130.9 | 76 | 73.58 | 73.70 | 8.03 | 8.12 |
| 1-Naphthyl | $C_{23}H_{26}N_2O_2$ | 362.46 | 105.8-106.5 | 80 | 76.21 | 76.00 | 7.23 | 7.19 |
| 4-Methoxyphenyl | $C_{20}H_{26}N_2O_3$ | 342.43 | 137-138 | 59 | 70.14 | 69.88 | 7.65 | 7.45 |

## TABLE II

## DATA ON 1-(2-CHLOROPHENYL)-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES

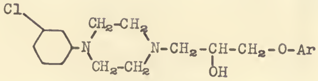


(Ar = Aryl Group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | C, % Calcd. | C, % Found | H, % Calcd. | H, % Found | N, % Calcd. | N, % Found |
|---|---|---|---|---|---|---|---|---|---|---|
| Phenyl | $C_{19}H_{23}N_2O_2Cl$ | 346.85 | 64-65 | 51 | 65.79 | 65.75 | 6.68 | 7.12 | -- | -- |
| 2-Chlorophenyl | $C_{19}H_{22}N_2O_2Cl_2$ | 381.30 | 99-100.5 | 35 | -- |  | -- |  | 7.35 | 7.53 |
| 4-Chlorophenyl | $C_{19}H_{22}N_2O_2Cl_2$ | 381.30 | 91.8-92.2 | 68 | 59.85 | 60.06 | 5.82 | 5.75 | -- |  |
| 2-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 76.7-77.7 | 41 | -- |  | -- |  | 7.59 | 7.41 |
| 3-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 64-65 | 57 | 66.56 | 66.71 | 6.98 | 7.04 | -- |  |
| 4-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 85.9-86.9 | 42 | -- |  | -- |  | 7.60 | 7.32 |
| 1-Naphthyl | $C_{23}H_{25}N_2O_2Cl$ | 396.91 | 124-124.6 | 75 | 69.60 | 69.69 | 6.35 | 6.20 | -- |  |
| 4-Methoxyphenyl | $C_{20}H_{25}N_2O_3Cl$ | 376.88 | 93-94 | 65 | 63.73 | 63.55 | 6.69 | 6.68 | -- |  |

## TABLE III

### DATA ON 1-(3-CHLOROPHENYL)-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES

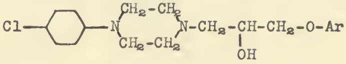


(Ar = Aryl Group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | C, % | | H, % | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Calcd. | Found | Calcd. | Found |
| Phenyl | $C_{19}H_{23}N_2O_2Cl$ | 346.85 | 85-86 | 68 | 65.79 | 65.69 | 6.68 | 6.51 |
| 2-Chlorophenyl | $C_{19}H_{22}N_2O_2Cl_2$ | 381.30 | 97-98 | 68 | 59.85 | 60.01 | 5.82 | 5.67 |
| 4-Chlorophenyl | $C_{19}H_{22}N_2O_2Cl_2$ | 381.30 | 109-109.7 | 72 | 59.85 | 59.87 | 5.82 | 5.74 |
| 2-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 95-95 | 71 | 66.56 | 66.26 | 6.98 | 6.62 |
| 3-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 80.5-81.5 | 62 | 66.56 | 66.47 | 6.98 | 7.01 |
| 4-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 92-93 | 61 | 66.56 | 66.87 | 6.98 | 7.01 |
| 1-Naphthyl | $C_{23}H_{25}N_2O_2Cl$ | 396.91 | 123-124 | 66 | 69.60 | 69.91 | 6.35 | 6.38 |
| 4-Methoxyphenyl | $C_{20}H_{25}N_2O_3Cl$ | 376.88 | 106.5-107.5 | 70 | 63.73 | 63.57 | 6.69 | 6.79 |

## TABLE IV

### DATA ON 1-(4-CHLOROPHENYL)-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES

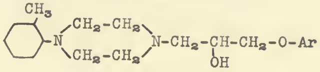


(Ar = Aryl Group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | C, % Calcd.<br>Found | H, % Calcd.<br>Found |
|---|---|---|---|---|---|---|
| Phenyl | $C_{19}H_{23}N_2O_2Cl$ | 346.85 | 130.8-131.4 | 69 | 65.79<br>65.89 | 6.68<br>6.68 |
| 2-Chlorophenyl | $C_{19}H_{22}N_2O_2Cl_2$ | 381.30 | 111.5-112.5 | 79 | 59.85<br>60.17 | 5.82<br>6.05 |
| 4-Chlorophenyl | $C_{19}H_{22}N_2O_2Cl_2$ | 381.30 | 154-155 | 53 | 59.85<br>59.88 | 5.82<br>5.98 |
| 2-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 93-94 | 48 | 66.56<br>67.02 | 6.98<br>6.98 |
| 3-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 106.3-106.6 | 67 | 66.56<br>66.67 | 6.98<br>7.22 |
| 4-Methylphenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 144-145 | 50 | 66.56<br>66.75 | 6.98<br>7.23 |
| 1-Naphthyl | $C_{23}H_{25}N_2O_2Cl$ | 396.91 | 125.3-126 | 53 | 69.60<br>69.70 | 6.35<br>6.40 |
| 4-Methoxyphenyl | $C_{20}H_{25}N_2O_3Cl$ | 376.88 | 143.5-144.5 | 68 | 63.73<br>69.90 | 6.69<br>6.50 |

## TABLE V

### 1-(2-METHYLPHENYL)-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES

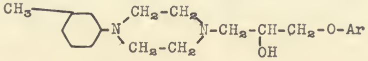


(Ar = Aryl Group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | C, % | H, % | N, % |
|---|---|---|---|---|---|---|---|
| | | | | | Calcd.<br>Found | Calcd.<br>Found | Calcd.<br>Found |
| Phenyl | $C_{20}H_{26}N_2O_2$ | 326.42 | 83.6-84.6 | 48 | -- | -- | 8.58<br>8.68 |
| 2-Chlorophenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 83-84 | 42 | -- | -- | 7.60<br>7.65 |
| 4-Chlorophenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 94-95 | 20 | 66.56<br>66.72 | 6.98<br>7.26 | -- |
| 2-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 80.8-82.3 | 38 | -- | -- | 8.23<br>8.29 |
| 3-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 57.1-58.6 | 36 | -- | -- | 8.23<br>8.30 |
| 4-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 75.8-76.3 | 45 | -- | -- | 8.23<br>8.19 |
| 1-Naphthyl | $C_{24}H_{28}N_2O_2$ | 376.48 | 84.8-85.2 | 41 | 76.56<br>76.31 | 7.50<br>7.63 | -- |
| 4-Methoxyphenyl | $C_{21}H_{28}N_2O_3$ | 356.45 | 100-100.5 | 52 | 70.76<br>70.53 | 7.92<br>8.03 | |

## TABLE VI

### DATA ON 1-(3-METHYLPHENYL)-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES

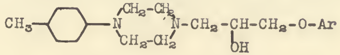


(Ar = Aryl Group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | C, % Calcd. Found | H, % Calcd. Found |
|---|---|---|---|---|---|---|
| Phenyl | $C_{20}H_{26}N_2O_2$ | 326.43 | 83.5-84.2 | 55 | 73.58<br>73.53 | 8.03<br>7.91 |
| 2-Chlorophenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 79.9-80.5 | 48 | 66.56<br>66.20 | 6.98<br>6.77 |
| 4-Chlorophenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 113.8-114.1 | 59 | 66.56<br>66.19 | 6.98<br>7.05 |
| 2-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 81-82 | 41 | 74.08<br>73.97 | 8.29<br>8.29 |
| 3-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 77-77.8 | 58 | 74.08<br>73.51 | 8.29<br>8.26 |
| 4-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 92.7-93 | 58 | 74.08<br>73.75 | 8.29<br>8.26 |
| 1-Naphthyl | $C_{24}H_{28}N_2O_2$ | 376.48 | 96.2-96.8 | 70 | 76.56<br>76.38 | 7.50<br>7.70 |
| 4-Methoxyphenyl | $C_{21}H_{28}N_2O_3$ | 356.45 | 100-100.5 | 62 | 70.76<br>70.53 | 7.92<br>8.03 |

## TABLE VII

### DATA ON 1-(4-METHYLPHENYL)-4-(2-HYDROXY-3-ARYLOXYPROPYL)PIPERAZINES



(Ar = Aryl Group)

| Aryl Group (Ar) | Molecular Formula | Molecular Weight | Melting Point | Yield % | C, % Calcd.<br>Found | H, % Calcd.<br>Found |
|---|---|---|---|---|---|---|
| Phenyl | $C_{20}H_{26}N_2O_2$ | 326.43 | 119-119.5 | 70 | 73.58<br>73.69 | 8.03<br>8.14 |
| 2-Chlorophenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 87-87.5 | 55 | 66.56<br>66.36 | 6.98<br>7.05 |
| 4-Chlorophenyl | $C_{20}H_{25}N_2O_2Cl$ | 360.88 | 137.8-138.6 | 55 | 66.56<br>66.69 | 6.98<br>7.11 |
| 2-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 97.3-97.8 | 56 | 74.08<br>73.76 | 8.29<br>8.61 |
| 3-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 85.6-86.5 | 57 | 74.08<br>74.06 | 8.29<br>8.27 |
| 4-Methylphenyl | $C_{21}H_{28}N_2O_2$ | 340.45 | 126-126.7 | 56 | 74.08<br>73.93 | 8.29<br>8.35 |
| 1-Naphthyl | $C_{24}H_{28}N_2O_2$ | 376.48 | 106.8-107.3 | 57 | 76.56<br>76.47 | 7.50<br>7.56 |
| 4-Methoxyphenyl | $C_{21}H_{28}N_2O_3$ | 356.45 | 130-131 | 63 | 70.76<br>70.69 | 7.92<br>7.97 |

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Jaime B. Fernandez was born June 10, 1929, in Tampa, Florida. He graduated from Hillsborough High School in Tampa in January, 1946. In 1947 he entered the University of Florida and was awarded the degree of Bachelor of Chemical Engineering in August, 1951. In the fall of 1951 he began graduate studies in chemistry at the University of Florida.

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This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of the committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

January 28, 1956

C. F. Byers
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